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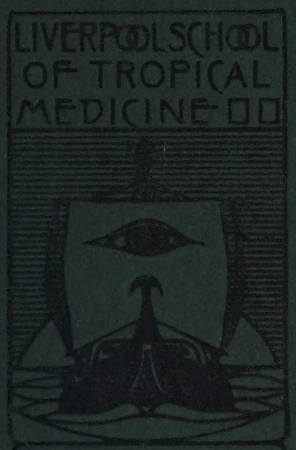

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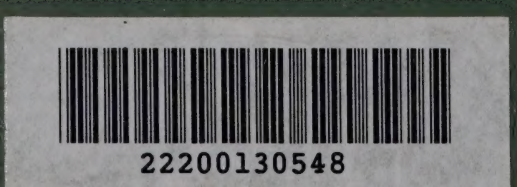
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A CASE OF MALARIAL FEVER, SHOWING A TRUE PARASITIC RELAPSE, DURING VIGOROUS AND CONTINUOUS QUININE TREATMENT

BY

SIR RONALD ROSS, K.C.B., F.R.S.

AND

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In the 'Annals of Tropical Medicine and Parasitology,' Vol. V, No. 3, December 30, 1911, we described the occurrence of pseudo or non-parasitic relapses in 6·7 % of our cases of malarial fever, during active quinine treatment of ten grains thrice daily. We were unable to prove that these 'pseudo-relapses,' which usually took the form of a sudden and isolated rise of temperature, had any connection with the original fever, as similar inexplicable rises of temperature occurred in 17 % of other diseases, during treatment in hospital.

Cases of malarial fever, resistant to quinine treatment, and which showed relapses during the treatment have been reported to occur in the Amazon region. During our experience of two years of careful observations on cases of malaria, we found no case which showed any resistant tendency to quinine, and twenty of these cases had contracted fever up the River Amazon. We, therefore stated in our paper (1911) that it was possible that these so-called resistant cases might have been cases of pseudo-relapses, especially as no data had been given with regard to the finding of parasites in them. We are now able, however, to confirm these reports, having observed carefully a case which showed marked resistance to quinine, and which showed a true parasitic relapse during treatment with that drug.

The details of this remarkable case, of which we publish a chart, are as follows:—

Patient E. E., age 65. Half-caste, born in Canada. Occupation, seaman.

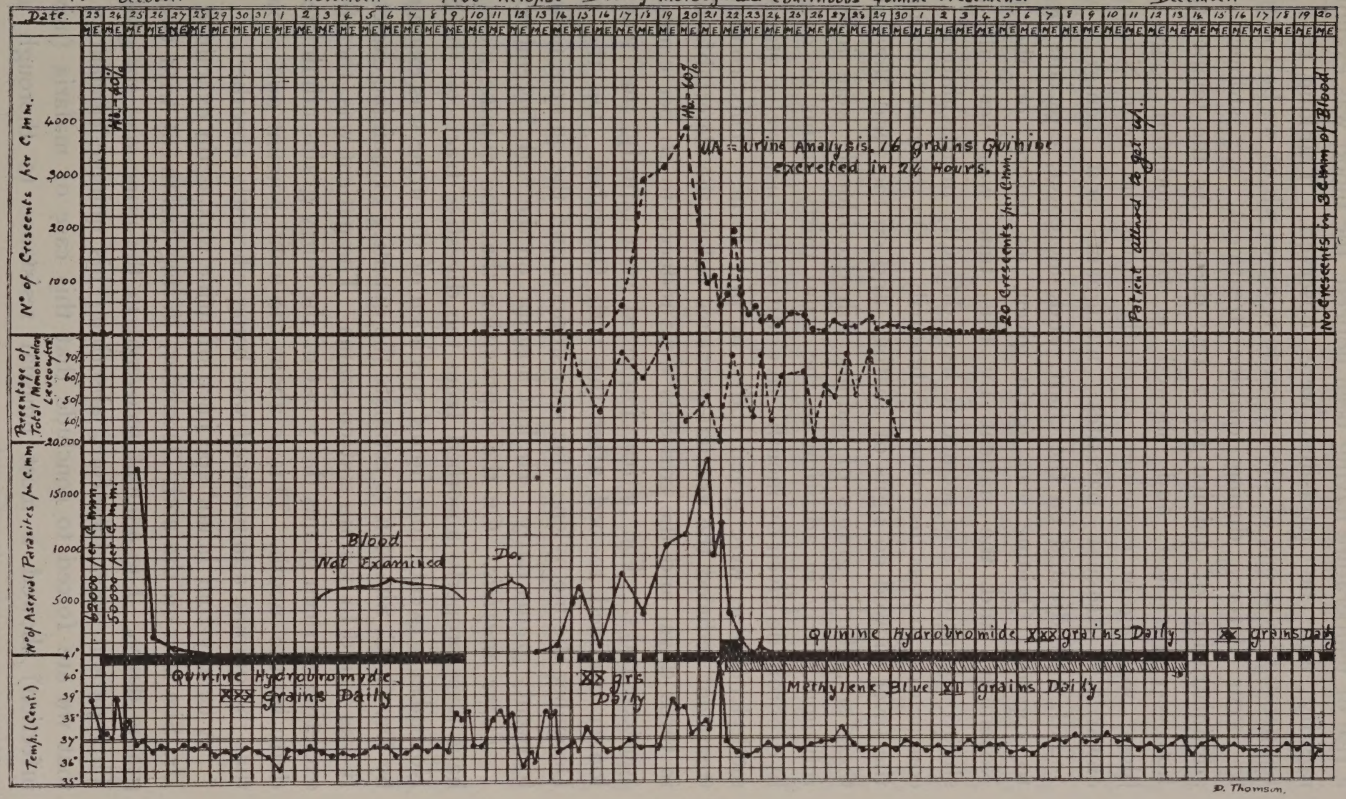
History prior to admission. Patient had been to sea for forty-five years, and had sailed to most parts of the world, including India, Japan, etc. He had a slight attack of malarial fever six years ago, but it did not trouble him much. In May, 1911, patient sailed up the Amazon river for the first time. He arrived at Porto Vellho on 17th May, 1911. There he left the ship and took a post ashore as foreman of a gang of labourers. He got an attack of fever on the 2nd of June, and was very ill, and states that he had dysentery as well. He was in bed for a month and was getting quinine thrice daily all the time. After this he remained well for two months, during which period he had quinine, according to his own statement, 'only once in awhile.' He had a second attack of fever in September, but this attack was not quite so severe. He then sailed down the river to Manaos and took a ship to England. He was ill during the whole of this voyage and got quinine only once or twice a week. He was admitted to the Tropical Ward of the Royal Southern Hospital, under our care on the 23rd October, 1911. The duration of his illness before admission was, therefore, 159 days.

Details of case after admission. These are shown graphically on the accompanying chart. On admission patient had fever, and the blood examination revealed a mixed infection of benign and malignant tertian malaria. A few crescents were present (about 16 per c.mm.) The blood showed marked auto agglutination of the red cells and nucleated and stipuled basic red cells were numerous. The haemoglobin was only 40%. There was no appreciable enlargement of the liver or spleen. The patient was very weak and somewhat emaciated, and had a tendency to be slightly delirous and incoherent in his speech.

Quinine hydrobromide in liquid form was administered in doses of ten grains thrice daily, by mouth. This reduced the asexual parasites to below the detectable limit in thin films, in five days, that is, about two days longer than usual. This dosage of quinine was continued for seventeen days, during which period the temperature remained normal. From the 3rd till the 9th November the blood was not examined; on the 10th November, however,

E.E. age 65 P. falciparum + P. vivax. (Amazon)

1337 October. November. True Relapse During thorough and Continuous Quinine Treatment. December.


Date
N° of Crescents per C.mm.
Percentage of Total Mononuclear Leucocytes
N°of Asexual Parasites per C.mm.
Temp. (Cent.)
Mk. 40%
Mk. 60%
UA = Urine Analysis. 16 grains Quinine excreted in 24 Hours.
20 Crescents per cmm.
Patient admitted 8 Dec 07.
No Crescents in 32 cmm of Blood
Blood Not Examined
Do.
Quinine Hydrobromide XXX grains Daily
XX grs. Daily
Quinine Hydrobromide XXX grains Daily
XX grains Daily
Methylene Blue XII grains Daily
D. Thomson.

a rise of temperature having been noticed, the blood was examined rapidly and no parasites were observed. Thinking that the temperature was one of those pseudo-relapses which we had noticed to occur before, during quinine treatment, we stopped the administration of quinine for a few days. As the temperature, however, persisted and showed a true malarial type, the blood was again examined carefully from the 14th November onwards. Asexual parasites, malignant and benign, were found, as indicated on the chart, and, moreover, crescents began to appear. Quinine was again given, as before, on the 14th November, and the patient by this time was very ill and slightly delirious, and seemed to have difficulty in articulation. He commenced to pass his urine involuntarily. On the 21st November, the fever showed no signs of abating, and on the 22nd November, therefore, thirty grains of quinine bihydrochloride were injected intramuscularly in addition to the usual thirty grains of quinine hydrobromide given by mouth. In addition to this, twelve grains of methylene blue were given daily in pill form. This combined treatment reduced the asexual parasites below the detectable limit in three days, and the crescents were reduced to 20 per c.mm. in fourteen days. The patient improved very rapidly, and was no longer confined to bed after the 10th December. On the 13th December the methylene blue was stopped and the quinine reduced to twenty grains daily. He left hospital on the 20th December.

Urine anaylsis. On the supposition that the quinine may not have been properly absorbed from the digestive tract, on the 21st November a twenty-four hours' specimen of the urine was examined by Dr. G. C. Simpson to estimate the quantity of quinine excreted. It was found to contain sixteen grains. The patient was, therefore, excreting thirteen grains daily out of the thirty grains administered daily by the mouth. This is about the usual amount and showed that the quinine administered was being efficiently absorbed.

A twenty-four hours' specimen of urine was again examined by Dr. Simpson on the 20th December, during treatment with twenty grains daily. The amount recovered in the urine was six grains. This patient was, therefore, absorbing his quinine efficiently, so that we are forced to conclude that this case of malaria (mixed infection) showed a most unusual resistance to thorough and continuous quinine treatment.

Before concluding we would like to remark that, though this patient was a weak old man of 65, yet in spite of a practically continuous treatment with quinine (thirty grains daily) for fifty days, he had no symptoms of deafness, nor did he complain of any of the symptoms of quininism. It has been our practice to give every case of malaria coming under our care ten grains of quinine thrice daily for a period of three weeks, and out of 200 cases treated in this manner, during the past two years, we have had few or no complaints of quininism produced by this so-called severe treatment. During such treatment the patients improve in health most markedly. They gain weight rapidly, and the haemoglobin percentage rises very quickly. They have always been able to hear well, and during convalescence they were able to work well in the ward. It is, however, not advisable to inform the patient as to the quantity of quinine that is being administered. It would appear that the majority of patients felt no more inconvenience from doses of thirty grains daily, than from doses of ten grains daily, after the first few days of administration.

CONCLUSIONS

(I.) A case of malaria, mixed infection (malignant tertian and benign tertian), contracted at Porto Vellho, River Amazon, has come under our care, shewing most unusual and marked resistance to quinine, and also a true parasitic relapse during thorough treatment with that drug.

(II.) Patients can tolerate, with very little discomfort, much more quinine than is generally supposed, especially when they are not aware that they are receiving heroic treatment.

REFERENCES TO LITERATURE

Ross & D. Thomson (1911). 'Pseudo-Relapses in Cases of Malarial Fever during Continuous Quinine Treatment.' Ann. Trop. Med. and Parasitol., Dec., V, 3, pp. 409-412.

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